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A case report of the Rifampin-warfarin drug interaction

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Abstract

The drug interactions of Warfarin and Rifampicin are commonly seen but not well known Rifampicin has been reported to increase the dose of Warfarin, hence there is strict need to maintain the dose of Warfarin that is 20 Mg/day to get the desired therapeutic effect of warfarin (anticoagulant) If the Rifampicin is withdrawn from the treatment chart, it will reduce the Warfarin requirement by 50% Rifampicin has the potential to induce the hepatic enzyme cytochrome P450 (CYP) and Warfarin is metabolised by enzyme cytochrome P-450 (CYP) hence increases the risk of drug-drug interactions. When these both drugs ie Rifampicin and Warfarin are co-administered then the therapy shall be continuously Monitored by (INR) International Normalized Ratio. Significant increase in warfarin doses are more likely seen. This case report focuses on termination of the co-administration of Rifampicin and Warfarin.

Keywords: Drug interactions, warfarin, rifampicin, cytochrome p450, international normalized ratio

Introduction

Rifampicin is one of the first-line drugs used in tuberculosis (TB). Rifampicin has the potential to induce the hepatic enzyme cytochrome P450 and the P-glycoprotein transport system increases the risk of drug-drug interactions. There are several well-documented examples of clinically significant drug-drug interactions during rifampicin therapy, including interactions between warfarin and rifampicin. But due to presence of co-morbidities we have to use multiple drug regimen. Due to co-administration of rifampicin and warfarin may lead to adverse drug events. Warfarin is the most common oral anticoagulant presently used. It is a coumarin derivative that is widely used to prevent and treat thromboembolic disorders It is used in treatment of patient suffering from chronic atrial fibrillation, deep venous thrombosis, pulmonary embolism, and dilated cardiomyopathy. It has led to widespread exposure to this drug ^[1].

The most common indication for warfarin are atrial fibrillation, prosthetic heart valves and venous thromboembolism ^[2].

The drugs may interact with warfarin through pharmacokinetics and pharmacodynamic mechanism. The drug that may interact with warfarin through pharmacodynamic include alteration of the bioavailability of Vit-K by antibiotics, mineral oils or cholestyramines, diuretics and hypolipidaemic agents like Clofibrate may influence Vit-K dependent clotting factor synthesis. The drugs which effects hemostasis will enhance anticoagulant effect of warfarin ^[3].

Pharmacodynamic interaction requires the knowledge by the prescriber for predicting interactions with warfarin and by International Normalised Ratio (INR) monitoring. Pharmacokinetic interaction can be monitored by using International Normalised Ratio level ^[2].

Overdose of the oral anticoagulant warfarin or its drug interaction may lead to toxicity ^[1].

Warfarin is a highly efficacious oral anticoagulant, but its use is limited by a well-founded fear of bleeding. Drug and food interactions are frequently cited as causes of adverse events with warfarin.

The number of drugs reported to interact with warfarin continues to expand. While most reports are of poor quality and present potentially misleading conclusions, the consistency of reports of interactions withazole antibiotics, macrolides, quinolones, no steroidal anti-inflammatory drugs, including selective cyclooxygenase-2 inhibitors, selective serotonin reuptake inhibitors, omeprazole, lipid-lowering agents, amiodarone, and fluorouracil, suggests

that co-administration with warfarin should be avoided or closely monitored [4].

International Normalised Ratio

The international normalized ratio (INR) is a standardized number which is calculated using the results of the prothrombin time (PT) test. Patients taking anticoagulants shall be monitored INR. This measures the time it takes for your blood to clot. INR levels should be maintained in order to avoid any further complications to the patient.

In healthy people an INR of 1.1 or below is considered normal. An INR range of 2.0 to 3.0 is generally an effective therapeutic range for people taking warfarin

Prothrombin is a protein made by the liver. It is one of several substances known as clotting factors. When you get a cut or other injury that causes bleeding, your clotting factors work together to form a blood clot. Clotting factor levels that are too low can cause you to bleed too much after an injury. Levels that are too high can cause dangerous clots to form in your arteries or veins.

A PT/INR test helps find out if your blood is clotting normally. It also checks to see if a medicine that prevents blood clots is working the way it should.

INR test is used to see how well warfarin is working. Warfarin is an anticoagulant which is used to treat and prevent blood clots in arteries & veins.

INR test is used to find out the reason for abnormal blood clots, INR test is used to find out the reason for unusual bleeding.

INR test is used Check clotting function before surgery Check for liver problems.

A PT/INR test is often done along with a partial thromboplastin time (PTT) test. A PTT test also checks for clotting problems.

This test is needed if the patient is taking warfarin on a regular basis. The test helps in taking the right dose.

Patients not on warfarin may also need this test if they have symptoms of a bleeding or clotting disorder.

Symptoms of a bleeding disorder include:

- Unexplained heavy bleeding
- Bruising easily
- Unusually heavy nose bleeds
- Unusually heavy menstrual periods in women.

In addition, you may need a PT/INR test if you are scheduled for surgery. It helps make sure your blood is clotting normally, so you won't lose too much blood during the procedure [5].

Case report

A 62 years old women was diagnosed with Atrial Fibrillation in 26 April 2021, warfarin therapy was given to her with INR range of 2.0-3.0.

Weekly warfarin dose was 54 mg/week. The patient medical history included HTN, DM. patient doesnot have any social habits such as smoking, alcohol consumption her past medication also included Telmisartan, mertformin Hcl, ace inhibitor captopril.

When the patient was taking therapy from the outpatient department, on 22 may 2021 she was diagnosed with T. Band begun the treatment with Isoniazid (400 mg/day), rifampicin (600 mg/day), pyrazinamide (2 g/day). INR values was obtained for several weeks after starting the anti-tubercular

therapy. Warfarin Doses were evaluated and adjusted accordingly, the Warfarin dose was increased gradually from 45mg/ week upto 80 mg /week.

It took 3 months to reach a stable INR and was maintained for another 3 months. On 20November 2021 anti-tubercular therapy was discontinued and therapeutic INR of 2.50 was obtained later that week. On dec 5 2022 patient noticed heavy bleeding in urine for 5 days and INR level was (7.0). Warfarin dose was stopped for 2 days, and weekly dose was reduced from 80 mg/week to 52 mg/ week.

A week after dose reduction pt's INR was 2.40. The patient had no history of bleeding. A complete Urine examination (CUE) was performed which shows no significant erythrocytes. Sequential INR values and warfarin weekly doses for Follow up are present in fig 1 graph.

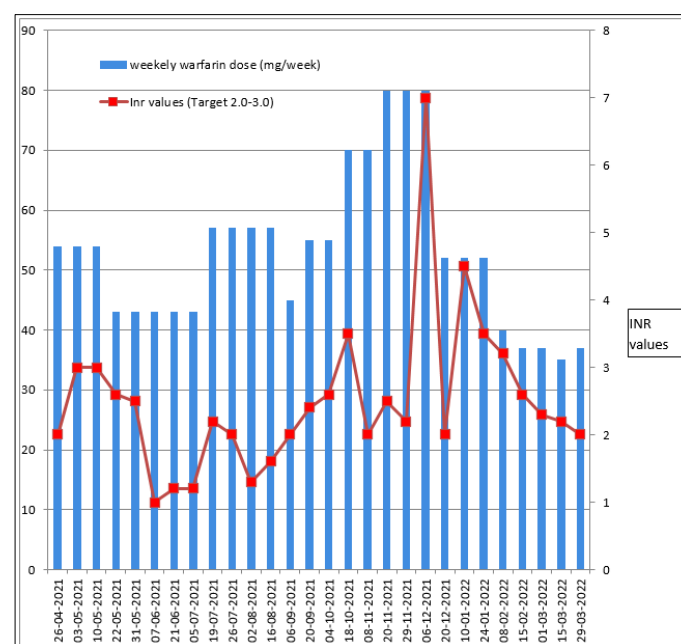


Fig 1: Sequential INR values and warfarin weekly doses

Conclusion

The case report shows the effect of Rifampicin on Warfarin. By increasing the requirement of warfarin dose. Hence there is increased risk of bleeding. The INR shall be monitored until a stable dose is achieved after discontinuing Rifampicin therapy, to prevent the complications arising due to unstable INR values. Especially the anticoagulant therapy + anti Tubercular therapy is at a greater risk of Drug Interactions. By monitoring INR levels weekly and adjusting the Warfarin dose accordingly will significantly reduce the incidence of Drug interactions.

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